REMARKS

Claims 1 and 3-16 are pending. Applicants respectfully request reconsideration of the present application in view of the reasons that follow.

I. Rejection Under 35 U.S.C. § 112, First Paragraph

Claims 1 and 3-16 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. The basis of the rejection is presented on pages 5-9 of the Office Action. In summary, the Examiner asserts "[i]n the present instance, the claimed method [is] for use in detecting the presence of a selected microscopic pathogen in a sample wherein the width of the depressions for the surface of the substrate are on the order of the size of the selected pathogen. The specification does not teach the method of detecting a pathogen wherein the width of the depressions is specific for the pathogen of a specific size and the genus of **any** specific size of pathogen. Therefore, only the method of detecting a pathogen wherein the width of the depressions is specific for the pathogen with a specific size of 100 nm such as the VSV, but not the full breadth of the claim method meet the written description provision of 35 U.S.C. § 112, first paragraph." Office Action, pages 8-9 (emphasis in original). Applicants respectfully traverse this rejection.

Applicants respectfully submit that the application as filed fully supports the claimed method for use in detecting the presence of a selected microscopic pathogen in a sample. The element at issue ("the width of the depressions are on the order of the size of the selected pathogen") is an important aspect of the claimed invention and is part of the microstructures found in the detection region of the substrate employed in the claimed methods. To appreciate the support found throughout the specification, it is important to understand the function of the microstructures in the claimed invention.

According to the claimed methods, to selectively detect a particular microscopic pathogen, the microstructures include depressions having width and depth wherein the width and depth of the depressions are selected in size to align a liquid crystal material in contact with the depressions and the width and depth of the depressions are selected in size to be occupied by the pathogen to be detected. In order for the depressions to be selected in size to be occupied by the selected pathogen, the width of the depressions are on the order of the size of the pathogen. Thus, after applying the liquid crystal material to the detection region, the liquid crystal material will be aligned by the microstructures on the surface of the substrate in the absence of binding of pathogen particles to the surface of the substrate. As recited in the specification, "Where no particles are present on the surface, the liquid crystal material is aligned and appears uniform and dark when visually examined." Page 8, lines 19-21. In the presence of the pathogen to be detected, the pathogen will bind to the binding agent and at least partially occupy the depressions. As explained in the specification, "The occupation of the depressions by the particles disrupts the uniform alignment of the liquid crystal material, with the result that the detection region appears relatively brightly colored when viewed with the appropriate polarizing material." Page 8, lines 24-26. Moreover, "[t]he depressions on the substrate are sufficiently large compared to molecular materials such as proteins which may be bound to the surface, and thus the non-specific binding of proteins or other molecular materials does not disrupt the uniform alignment of the liquid crystal material." Page 8, line, 28 through page 9, line 2. Accordingly, Applicants respectfully submit that the basis for the ability to visually detect the selected pathogen relies in part on the width of the depressions being on the order of the size of the selected pathogen as well as being able to align the liquid crystal material contacting the depression.

If the depressions are not on the order of the size of the selected pathogen, the method will not operate properly. For example, if the depression is too small, the individual pathogen particles will not fit at least partially into the depression and occupy the depression. Therefore, no visibly observable disordering of the liquid crystal material will take place when the liquid crystal material is applied to the detection region. If the width of the depression is too large

compared to the pathogen to be detected, sensitivity will be degraded as the width of the depression increases because the disordered areas of the liquid crystal material becomes a smaller fraction of the total liquid crystal material in the depressions thereby obscuring the observable disordering of the liquid crystal material. The invention thus functions optimally, as claimed, when the width of the depressions is on the order of the size of the selected pathogen.

The following excerpts from the application clearly support the language at issue. First, the Summary notes that "The depressions are also sized to be occupied by the pathogen to be detected. The depressions may comprise parallel microgrooves. For detection of viruses, the width and depth of the microgrooves will generally be on the order of 5 nm to 500 nm, while for detection of bacteria the width and depth of the microgrooves would generally be on the order of 0.1 μm to 10 μm." Page 7, lines 23-27 (emphasis added). As one of skill in the art will readily appreciate, these size ranges are given to illustrate that viruses and bacteria generally fall into different size ranges and will thus require appropriately sized depressions. Thus, one of ordinary skill in the art will readily understand that the size of the depressions will vary with the size of the pathogen to be detected. Indeed, the very language "on the order of" is expressly presented here and teaches that the sizes for the depressions which are generally appropriate for detection of pathogens such as viruses and bacteria depends on whether the pathogen to be detected is viral or bacterial.

Even more clearly, the Detailed Description states, "the width of the grooves is preferably selected to be about the size of an individual pathogen particle, so that the particle will fit at least partially into a groove to occupy the groove." Page 13, lines 27-29 (emphasis added). The reason for this size dependence is explained: "The size of the grooves and the spacing of the grooves are also selected such that adherence of a pathogen particle or clumps of particles of the appropriate size will disrupt the uniform orientation of the liquid crystal material, causing a visible change in the appearance of a liquid crystal to signal the detection of the virus to an observer." Page 13, lines 14-18. In addition, the specification discloses the sizes that the depressions may not be; i.e., they must be sufficiently large so that "the non-specific binding of

proteins or other molecular materials does not disrupt the uniform alignment of the liquid crystal material." Page 8, line 28 through page 9, line 2.

The specification further teaches practical implications of the recited size relationship between the depressions and the pathogens to be detected. For example, the specification states that "the detection apparatus may be further embodied in that it contains two or more detection regions such that the detection regions have grooves of different widths, depths, or both such that the different regions of the detection apparatus have different sensitivities to a single specific pathogen." Page 8, lines 27-31. More specifically,

> [d]etection apparatus may also be constructed that include detection regions with different sensitivities toward the same pathogen. Such detection apparatus include at least a second detection region on the surface of the substrate. The second detection region has grooves with a width that is different from that in the first detection region; grooves with a depth that differs from those in the first detection region; or grooves with both a width and depth that differs from those in the first detection region. The difference in the dimensions of the grooves of different detection regions allows the microarray to be used where the suspected concentration of the target species is not well known because the concentration of pathogen which results in the disordering of the liquid crystals will differ depending on the width and depth of the grooves in the detection region.
> Page 19, lines 10-22

The specification also includes an example that illustrates, but does not limit, the invention: "[a]s shown in Fig. 3 for illustration, the size of the BSA and IgG molecules adhered to the surfaces to form the film 33 was small in comparison to the dimensions of the grooves 26. The dimensions of the grooves 26 were comparable in size to vesicular stomatitis virus (VSV) (typically virus size particle about 100 nm x 45 nm), a particle of which is shown for illustration at 35 in Fig. 3." Page 17, lines 5-9 (emphasis added). "The width of the grooves 26 in the substrate was 100 nm, which is on the order of the size of the VSV virus particle (about 100 nm x 45 nm), allowing the virus particle to at least partially fit into and occupy the groove." Page 18, lines 2-5 (emphasis added). Thus, the specification specifically sets forth that the width of

the grooves should be on the order of the size of the pathogen to be detected. Based on this and the other excerpts from the specification, one skilled in the art would definitely understand that the inventors were in possession of the claimed invention at the time the application was filed.

The Examiner asserts that "with the exception of the method of detecting a pathogen wherein the width of the depressions is specific for the pathogen with a specific size of 100 nm such as the VSV disclosed by the specification, the skilled artisan cannot envision the method of detecting a pathogen wherein the width of the depressions is specific for the pathogen of a specific size and the genus of **any** specific size of pathogen." Office Action, pages 7-8 (emphasis in original). Applicants respectfully disagree.

The wealth of excerpts from the specification that are provided above establish that the claimed element was clearly envisioned and possessed by the inventors at the time the application was filed. Clearly, the specification supports the claimed method utilizing depressions on the substrate where the width of the depressions is on the order of the size of the selected pathogen (as well as the other recited elements). Given this simple relationship and the detailed example set forth in the application for detection of VSV, it is not necessary or required that Applicants provide further examples of differently sized pathogens as the Examiner seems to suggest. Such data is well known to those of skill in the art and is publicly available in documents filed prior to the filing date of this application (see for example "Manual of Clinical Microbiology," 5th edition, Washington DC, 1991, pages 222, 258, 287, 296, 304, 442, 454, 471, 823, 838, 847, 860, 897, 905, 918, 924, and 963, a copy of which is enclosed for the convenience of the Examiner). Applicants are, therefore, not required to include it (see, e.g., Ajinomoto Co. v. Archer-Daniels-Midland Co., 228 F.3d 1338 (Fed. Cir. 2000) ("A patent is not a scientific treatise, but a document that presumes a readership skilled in the field of the invention.")). Moreover, the specification teaches specific methods for patterning substrates to ensure that the depressions on the substrate are sized according to the size of the pathogen to be detected. Thus, one skilled in the art will readily understand that the inventors had possession of the claimed methods because both the size relationship between the depressions on the substrate and the size

of the pathogen are disclosed, and the knowledge of pathogen sizes is well known to those of skill in the art. Accordingly, the claims are very well supported by the application as filed and have an adequate written description that complies with the requirements under the first paragraph of 35 U.S.C. § 112. Applicants, therefore, respectfully request that the Examiner reconsider and withdraw the rejection of claims 1, and 3-16 under the first paragraph of 35 U.S.C. § 112.

II. Rejection Under 35 U.S.C. § 102(e)

Applicants respectfully traverse the rejection of claims 1 and 3-16 under 35 U.S.C. § 102(e) for being allegedly anticipated by Abbott (U.S. Patent No. 6,284,197). The present invention as defined, for example, by claim 1, distinguishes over the cited reference by at least reciting a substrate having a detection region thereon comprising certain well defined microstructures (depressions), the width and depth of which are selected in size to align a liquid crystal material and to be occupied by the selected pathogen and in which the width of the depressions are on the order of the size of the selected pathogen. Claim 1 further distinguishes over the cited reference at least by reciting applying the liquid crystal material to the detection region that will be aligned by microstructures on the surface of the substrate in the absence of the binding pathogen particles to the surface of the substrate, wherein the presence of the selected pathogen bound to the binding agent and at least partially occupying the depression would be manifested by a visually observable disordering of the liquid crystal material. The Abbott reference simply does not teach each of these elements and therefore cannot anticipate the present invention.

First, Abbott fails to teach or suggest the specific relationship in size between the depressions of the detection surface and the pathogen to be detected as claimed in the present methods. Applicants respectfully contend that the Examiner's assertion on page 5 of the Office Action that Abbott does "suggest that the size relationship between the depressions and biomolecule to be detected" is misplaced. The fact that "an analyte, or other substance, placed in a particular well remains substantially confined to that well" reveals nothing about any size

relationship between the analyte and the well. A bushel of apples may be confined to the bushel basket, but that does not mean the bushel basket is on the order of the size of the apple. Nor does it provide any reason for using a basket on the order of the size of an individual apple. It is clear from examination of the following entire paragraph in which the quoted sentence appears that size has nothing to do with this statement:

> In a presently preferred embodiment, the patterning is used to produce a substrate having a plurality of adjacent wells, wherein each of the wells is isolated from the other wells by a raised wall or partition and the wells do not fluidically communicate. Thus, an analyte, or other substance, placed in a particular well remains substantially confined to that well. In another preferred embodiment, the patterning allows the creation of channels through the device whereby an analyte can enter and/or exit the device. Abbot, col. 17, lines 19-27.

Applicants respectfully contend that the cited paragraph set forth above is directed to wells in which the analyte may be manually placed such as by using a pipette or other delivery device. While the analyte must fit in the well, there is no teaching that the size of the well should be on the order of the size of the analyte. Nor does the cited paragraph or any other in the specification disclose why one would wish to have such a size relationship. Rather, the paragraph as a whole emphasizes that the wells containing the analyte do not "fluidically communicate" with each other unless channels are created between them. There is no express or inherent teaching that the wells should be of a particular size that will both cause a liquid crystal material to be aligned and exhibit a visually observable disordering of a liquid crystal material when a bound pathogen is present.

Similarly, the statement "the size and complexity of the pattern on the substrate is limited only by the resolution of the technique utilized and the purpose for which the pattern is intended" referred to on pages 4 (lines 7-9) and 5 (lines 10-12) of the Office Action and set forth in column 17, lines 7-9 of Abbott fails to teach any more than that one can make a wide variety of patterns on the substrate. It says nothing about what pattern one would want to make, nor what size that

pattern should be, nor why it should be a particular size. Specifically, these statements cited by the Examiner do not teach a detection region having depressions that are specifically sized based on both the size of a desired pathogen to be detected and on the ability to align a liquid crystal materials placed thereon.

Likewise, the Examiner has failed to point to any teaching in Abbott in which microstructures are utilized to align a liquid crystal material in contact therewith. In fact, the Examiner's own description of the method of Abbot which follows highlights the differences from the present method:

> the analyte (pathogen) first interacts with the recognition moiety (binding agents) and the mesogenic layer (liquid crystal) is introduced in its isotropic phase. The mesogenic layer is subsequently cooled to form the liquid crystalline phase. The presence of tie analyte within regions of the mesogenic layer will disturb the equilibrium between the nematic and the isotropic phases leading to different rates and magnitudes of nucleation at those sites.
> Office Action, page 3, lines 10-15.

The method of Abbott simply has no need for microstructures which align a liquid crystal material and does not require or disclose that binding of a pathogen to the binding agent in the microstructure will lead to a visually observable disordering of the liquid crystal material based on the size of the microstructure. Nowhere in the discussion of substrate surfaces (col. 16, line 46 through col. 17, line 60) or elsewhere in the patent does Abbott disclose that the width and depth of the depressions are selected in size to align a liquid crystal material in contact therewith.

Accordingly, Applicants respectfully submit that Abbott neither teaches nor suggests all of the claimed elements or their arrangement and cannot anticipate the present invention. Because Abbott does not teach or suggest each of the claim elements, the rejection must fail. Applicants, therefore, respectfully request that the Examiner reconsider and withdraw the rejection of claims 1 and 3-16 under 35 U.S.C. § 102(e).

CONCLUSION

In view of the above remarks, reconsideration and favorable action on all claims is respectfully requested. If any issues remain to be resolved in view of this response, the Examiner is invited to contact the undersigned at the telephone number set forth below so that a prompt disposition of this application can be achieved.

Respectfully submitted,

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